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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/762,040	01/21/2004	Jeff Yon	BWT-004 US	3915
48329	7590	02/26/2009		
FOLEY & LARDNER LLP 111 HUNTINGTON AVENUE 26TH FLOOR BOSTON, MA 02199-7610			EXAMINER NOAKES, SUZANNE MARIE	
			ART UNIT 1656	PAPER NUMBER
			MAIL DATE 02/26/2009	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/762,040

Applicant(s)

YON ET AL.

Examiner

SUZANNE M. NOAKES

Art Unit

1656

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 August 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-87 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) _____ is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 1-87 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SF/ICE)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:
 - I. Claims 1-8, 14-25, 59 and 60, drawn to a BACE protein crystals and polypeptides, classified in class 436, subclass 4.
 - II. Claims 9-11, 45, 46, 69 and 70, drawn to a method of ligand screening by using a BACE protein crystal to determine ligand-BACE binding, classified in class 435, subclass 4.
 - III. Claims 12, 47 and 71, drawn to a computer assisted method of identifying potential ligands of a BACE by using a three-dimensional structure of said BACE, classified in class 703, subclass 11.
 - IV. Claims 13, 48, 51-55, 67, 72 and 74-76, drawn to ligands/modulators of BACE and compositions thereof, classified in class 506, subclass 13.
 - V. Claims 26-41 and 61-66, drawn to nucleic acids encoding various BACE polypeptides, vectors, kits contains said vectors and methods of expressing the polypeptide, classified in class 536, subclass 23.1.
 - VI. Claim 44, drawn to a method of determining the crystal structure of a BACE protein by obtaining X-ray diffraction patterns of said BACE, classified in class 702, subclass 27.
 - VII. Claims 49 and 73, drawn to an assay to determine which compounds are ligands or modulators of BACE, classified in class 435, subclass 4.

- VIII. Claims 50 and 68, drawn to an antibody of BACE, classified in class 530, subclass 387.9.
- IX. Claims 56-58, 77 and 78, drawn to a method of inhibiting BACE or the production of A β or treating AD in an individual by administering an inhibitor/modulator of BACE, classified in class 514, subclass 12.
- X. Claim 79-84, drawn to use of a BACE inhibitor or modulator to make a medicament, classified in class 514, subclass 1.
- XI. Claims 85 and 86, drawn to a computer system for generating structures of BACE and a computer readable medium containing said data to generate said structures, classified in class 708, subclass 800.
- XII. Claim 87, drawn to a method of doing business by using the computer structure having the three-dimensional structure of BACE stored therein, classified in class 705, subclass 500.

The inventions are distinct, each from the other because of the following reasons:

- 2. Inventions I and II/VI/VII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case the method of ligand screening using a BACE protein crystal does not necessarily have to use the product of Group I; rather, one skilled in the art can use the product of Hong et al. (see

Science, 2000, 290:150-153 – cited on IDS 03/23/2005) to use in said screening method.

3. Inventions I and III/XI/XII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not related because the *in silico* method of identifying ligands/modulators of BACE, and the computers which are used in the *in silico* aspect of said method Groups III/XI/XII does not directly use the product of Groups I. Instead Groups III utilizes the atomic coordinates of BACE in the design process which is confined within a computer readable storage medium containing said atomic coordinates and is only related to the crystal product of Group I by utilizing non-functional descriptive material to establish a tangible pictorial representation of the physical atomic level structure. Thus the Groups are not directly utilizable together, nor are disclosed as being capable as such.
4. Inventions I and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the inhibitors/modulators have a completely difference physical structure (albeit complementary) to that of the protein crystal and said protein contained within said crystal. As such, a search would not necessarily be coextensive and place an undue search burden upon the Examiner.

5. Inventions I and V are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the DNA of Group V is related to the protein of Group I by virtue of the fact that the DNA may code for the protein. The DNA molecule has utility for the recombinant production of the protein in a host cell. Although the DNA and the protein may be related, they are distinct inventions because the protein product can be made by other and materially distinct processes, such as purification from the natural source or chemical synthesis. Further, DNA can be used for processes other than the production of protein, such as nucleic acid hybridization assays.

Furthermore, searching the inventions of Groups I and V together would impose a serious search burden. In the instant case, the search of the polypeptides and the polynucleotides are not coextensive. The inventions of Groups I and II have a separate status in the art as shown by their different classifications. In cases such as this one where descriptive sequence information is provided, the sequences are searched in appropriate databases. There is search burden also in the non-patent literature. Prior to the concomitant isolation and expression of the sequence of interest there may be journal articles devoted solely to polypeptides which would not have described the polynucleotide. Similarly, there may have been "classical" genetics papers which had no knowledge of the polypeptide but spoke to the gene. Searching, therefore is not coextensive. As such, it would be burdensome to search the inventions of Groups I and V together.

6. Inventions I and VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different inventions the protein of group I is related to the antibody of group VIII by virtue of being the cognate antigen necessary for the production of antibody. Although the protein and antibody are related due to the necessary steric complementarity of the two, they are distinct inventions because the protein can be used in other, materially different processes from the production of antibody such as in a pharmaceutical composition in its own right, or to assay or purify the natural ligand of the protein if it is a receptor. Further, a protein and its cognate antibody are structurally and functionally distinct molecules with different amino acid compositions.

7. Inventions I and X are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different inventions are not related because the protein/crystal is not used to make the medicament, the inhibitor of the protein is. Thus, the products are independent and distinct and there would not be an overlap in the expected search and thus there would be an undue search burden upon the Examiner.

8. Inventions II/VII and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different inventions the Groups are patently distinct methods because Group II practices

said method *in vitro* or *in vivo* with actual physical products whereas Group III method steps take place virtually. Thus, there would not be an overlap in the expected search and thus there would be an undue search burden upon the Examiner.

9. Inventions IV and II/III/VII/IX/X are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case the compounds or inhibitors as claimed can be used in other materially different process such as screening assays for the inhibition of other enzymes other than BACE.

10. Inventions V and II-IV/VI-XII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different inventions are all unrelated because none of the use the nucleic acids which encode BACE in any of the methods. Furthermore, the products are all materially different in design and thus there would be no coextensive search and an undue search burden on the Examiner.

11. Inventions II and VI are directed to related but distinct processes. The related inventions are distinct if: (1) the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect; (2) the inventions do not overlap in scope, i.e., are mutually exclusive; and (3) the inventions as claimed are not obvious variants. See MPEP § 806.05(j). In the instant

case, the inventions as claimed both utilize BACE protein crystals in the method steps, however, the method steps and end points all constitute patentably distinct and independent methods. Furthermore, there is nothing of record to show them to be obvious variants.

12. Inventions II and VII/IX/X are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different inventions are materially different methods which utilize different products in said method steps in order to produce different end points. As such, there would be no coextensive search and an undue search burden on the Examiner.

13. Inventions II and XI/XII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different inventions the method of screening ligands using BACE crystals do not overlap and cannot be utilized in any way in the computer systems or methods of doing business of Group XI and XII, respectively. As such, there would be no coextensive search and an undue search burden on the Examiner.

14. Inventions II and VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different inventions are unrelated as they are drawn to independent and distinct processes which arrive at different end points. For instance, the products used in the

method of Group VI do not require that the BACE proteins be in complex form. Thus, there would not necessarily be any overlap in the search of the two methods and there would be no coextensive search and an undue search burden on the Examiner

15. Inventions VIII and II-VII/IX-XII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different inventions are not related because the antibodies of Group VIII are not utilized in any of the methods and are structurally distinct from the products to such an extent there would be no expectation of coextensive search and thus an undue search burden upon the Examiner.

16. Inventions II and XI/XII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different inventions method of utilizing protein crystals in no way overlaps with either a computer storing data or methods of using said computer. As such, there would be no coextensive search and an undue search burden on the Examiner.

17. Inventions III and VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different inventions are unrelated because the methods utilize different products (e.g. date versus a protein crystal) in order to obtain the patentably distinct and independent

end points. As such, there would be no coextensive search and an undue search burden on the Examiner.

18. Inventions III and VII/IX/X are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06. In the instant case, the different inventions are materially different methods which utilize different products in said method steps in order to produce different end points. As such, there would be no coextensive search and an undue search burden on the Examiner.

19. Inventions III/XII and XI are related as process and apparatus for its practice. The inventions are distinct if it can be shown that either: (1) the process as claimed can be practiced by another and materially different apparatus or by hand, or (2) the apparatus as claimed can be used to practice another and materially different process. (MPEP § 806.05(e)). In this case the computer readable medium of Groups XI can be used for separate processes such as running software in order to create spreadsheets, write word documents, etc., or to run statistical analysis of sets of data.

20. Inventions IV and VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different inventions are unrelated and the products of Group IV are not necessary or even utilized for the methods of Group VI. As such, there would be no coextensive search and an undue search burden on the Examiner.

21. Inventions IV and XI/XII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the ligands of Group IV in no way overlaps with either a computer storing data or methods of using said computer. As such, there would be no coextensive search and an undue search burden on the Examiner.

22. Inventions VI and VII/IX/X are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different inventions are materially different methods which utilize different products in said method steps in order to produce different end points. As such, there would be no coextensive search and an undue search burden on the Examiner.

23. Inventions VI and XI/XII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the method of determining the crystal structure produces the data stored on the computer, however, the method does not directly use the computer with data already stored thereon. As such, there would be no coextensive search and an undue search burden on the Examiner.

24. Inventions VII and IX/X are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the

different inventions are materially different methods which utilize different products in said method steps in order to produce different end points. As such, there would be no coextensive search and an undue search burden on the Examiner.

25. Inventions VII and XI/XII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the assay to determine ligands of BACE of Group VII in no way overlaps with either a computer storing data or methods of using said computer. As such, there would be no coextensive search and an undue search burden on the Examiner.

26. Inventions IX and X are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different inventions are materially different methods which utilize different products in said method steps in order to produce different end points. As such, there would be no coextensive search and an undue search burden on the Examiner.

27. Inventions IX/X and XI/XII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the assay to determine ligands of BACE of Group VII in no way overlaps with either a computer storing data or methods of using said computer. As such, there would be no coextensive search and an undue search burden on the Examiner.

28. Restriction for examination purposes as indicated is proper because all these inventions listed in this action are independent or distinct for the reasons given above and there would be a serious search and examination burden if restriction were not required because one or more of the following reasons apply:

- (a) the inventions have acquired a separate status in the art in view of their different classification;
- (b) the inventions have acquired a separate status in the art due to their recognized divergent subject matter;
- (c) the inventions require a different field of search (for example, searching different classes/subclasses or electronic resources, or employing different search queries);
- (d) the prior art applicable to one invention would not likely be applicable to another invention;
- (e) the inventions are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a invention to be examined even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected invention.**

The election of an invention may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election

shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected invention.

If claims are added after the election, applicant must indicate which of these claims are readable upon the elected invention.

Should applicant traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

29. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Potential Right to Rejoinder

30. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are

subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

31. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUZANNE M. NOAKES whose telephone number is (571)272-2924. The examiner can normally be reached on 7.00 AM-3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SUZANNE M. NOAKES/
Primary Examiner, Art Unit 1656
20 February 2009